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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/601,997	KECK, JAMES G.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-14 and 58-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-14 and 58-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-26-07 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 112

3. Claims 9-14, and 58-73 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record, and for those reasons set forth below.

4. Applicant's arguments filed 9-26-2007 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks. Applicants argue that the "[Definiteness of claim language must be analyzed, not in a vacuum, but in light of 91) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the

interpretation claims would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Claims need only 'reasonably apprise those skilled in the art' of their scope and be 'as precise as the subject permits.'"

Contrary to Applicant's assertions, the instant claims do not reasonably apprise the skilled artisan the metes and bounds of the scope of the claimed invention. Instant claim 58 provides multiple conflicting descriptions of the oligonucleotide family members encompassed by the instant claim. In one instance, claim 58 recites: "[w]herein each member of the oligonucleotide family encodes a transcription product comprising a sequence that is complementary to ***a sequence contained in the mRNA transcribed from the target nucleic acid molecule*** that comprises the sample nucleic acid;" and in another instance the claim recites: "[w]herein the plurality of members of the oligonucleotide family are introduced into expression vectors, wherein the expression vectors comprise: double-stranded DNA, comprising: a sense strand and an antisense strand, wherein ***the sense strand encodes RNA that binds to an mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence*** so that expression of a product from the target nucleic acid is inhibited." In one instance the transcription product is complementary to ***a sequence*** contained in the mRNA transcribed from the target nucleic acid that comprises the sample nucleic acid, wherein the scope of the term ***a sequence,*** can include sequences that do not include the sample nucleic acid. In the second instance the claim encompasses wherein the oligonucleotide members are introduced into expression vectors comprising a double stranded region, wherein the ***sense strand*** encodes RNA that ***binds to an mRNA***

sequence transcribed from the sample nucleic acid in the target nucleic acid. Furthermore, there is a third instance wherein claim 58 recites wherein ***the coding sequence for each individual transcription product encodes an antisense that binds to the mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid.***

Finally, in part (b) of the claim Applicants recite that comparing the phenotypes of the resulting host cells to phenotypes of control cells to identify changes in phenotype to thereby assign ***a function associated with the product encoded by the sample nucleic*** acid sequence in the target nucleic acid. In order to achieve this final step, the members of the oligonucleotide family would unambiguously have to inhibit the expression of the mRNA transcribed from the sample nucleic acid comprised within the target nucleic acid. However, part (a) of the claim recites that the "transcription products" (*assuming that of the oligonucleotide family members*) can be complementary to "*a sequence that is complementary to a sequence contained in the mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid*" (see lines 13-16 of claim 58), and that "*the transcription product encodes an antisense that binds to the mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid*" (see lines 29-31 of claim 58). In both instances the claim language suggests that transcription product binds or encodes a product that binds a sequence other than the mRNA specifically transcribed from the "***sample nucleic acid***." As stated above, if it is unclear that the mRNA specifically produced from

the *sample nucleic acid* is not inhibited, then it is unclear if the objective of the claimed method can be achieved.

Moreover, in regards to Applicant's assertion that the claims, if read in light of the specification, reasonably apprise those skilled in the art of the utilization and scope of the invention, see MPEP § 2106[R-5].II.C which states:

> **>USPTO personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). ***Limitations appearing in the specification but not recited in the claim should not be read into the claim.*** E-Pass Techs., Inc. v. 3Com Corp., 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" ***without importing limitations from the specification into the claims unnecessarily***). In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... ***An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous***. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.")."

In the instant case, although the examiner recognizes that the claims are to be interpreted in light of the specification, it is noted that as stated above, "*[L]imitations appearing in the specification but not recited in the claim should not be read into the claim*," moreover, it is also stated above that when ambiguities are recognized that clarification should be imposed in an effort to fashion claims that are precise, clear, correct, and unambiguous. As stated above, the instant claims recite multiple and conflicting descriptions of the "transcription products" of the instant invention, such that the skilled artisan would not be reasonably apprised of the scope and nature of the

claimed invention.

Furthermore, claim 59 (and those claims dependent therefrom, claims 60-63, and 70), lines 2-4 recite "wherein the RNA that is produced from the sense strand of *(??)* binds to an mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence so that expression of a product from the target nucleic acid is inhibited." Again, lines 2-4 of claim 59 recites that a sense strand of (*?? unknown composition*) **binds** *an mRNA sequence transcribed from* ***the target nucleic acid,*** there is no requirement that mRNA transcribed from the target nucleic acid is necessarily equivalent to an mRNA sequence transcribed from the sample nucleic that is comprised within the target nucleic acid. Moreover, it is not clear that inhibiting an mRNA sequence transcribed from the target nucleic acid, necessarily results in the inhibition of an mRNA sequence transcribed from the sample nucleic acid.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 8-14, and 58-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. and Draper et al. (US 5,496,698) in view of Gudkov et al. (see PTO-892 of 02-03-2005)

The following prior art is applied to the extent that the instant claims are interpreted as encompassing wherein gene function is assigned based upon the observation of "changes in the phenotype" of non-bacterial cells expressing one or more members of an oligonucleotide family that function to inhibit the expression of an mRNA transcribed from a target nucleic acid sequence, in comparison to the phenotype of cells not expressing one or more members of an oligonucleotide family.

Wagner et al. teach methods to define gene function. In a particular embodiment of Wagner et al., ribozymes are transiently or stably transfected into a host cell, the effect of ribozyme expression on the transfected cell (e.g., fertilized egg cell, cell derived from a cell line, plant protoplast, callous cell, etc.) and/or progeny (e.g., embryo, fetus, adult animal, plant, subsequent generations of a cell line, etc.) derived from this cell is determined in relation to controls which are not transfected with the expression vector, or which are transfected with an expression vector that encodes an RNA which does not cleave the substrate RNA. For example, morphological and pathological changes may be determined using methods known in the art such as by visual inspection, histological staining, electron microscopy, magnetic resonance imaging (MRI), computerized tomography (CT) scans and the like. Morphological changes as a result of ribozyme expression indicate that the gene whose transcript is cleaved by the ribozyme is important in the formation of the structure whose morphology is altered by ribozyme expression. In a preferred embodiment, the observed change is morphological. (see col. Col. 29). Absent evidence to the contrary, the methods of Wagner et al. used to identify morphological and pathological changes would identify wherein the function of

associated with a particular product is associated with changes in enzyme activity or protein synthesis (i.e. histological staining), expression of a biological factor, or a regulatory effector function.

The invention of Wagner et al. may also be considered to encompass the use of antisense nucleic acid molecules to inhibit the expression of genes for the expressed purpose of determining gene function, since the structure of the ribozymes described by Wagner et al. include two antisense oligonucleotide regions which function to bind the substrate nucleic acid (see page 17, line 58). Therefore, the ribozyme constructs of Wagner et al. may be considered to encompass antisense nucleic acid. Transfection of the ribozyme constructs of Wagner et al. is not limited to the use of plasmids as vectors. Other expression vectors contemplated to be within the scope of the invention include, but are not limited to, recombinant bacteriophage, cosmid DNA expression vectors, yeast expression vectors, virus expression vectors and the like (see col. 25-26). The invention of Wagner et al. may also encompass the use of a retroviral vector to infect cells with the nucleic acid constructs encoding the inhibitory nucleic acid molecules of the invention (see col. 10, line 24).

7. Draper, U.S. Patent No. 5,496,698, (at col. 1-3 and 10) discloses identifying one or more members of a combinatorial ribozyme library comprising contacting a *mammalian cell culture* with members of the library which bind to and disrupt a transcription product and identifying host cells that exhibit phenotypic changes, whereby members of the combinatorial library are identified; wherein the identified members are used as a probe to identify nucleotide sequences; and wherein the transcription product

is mRNA. Draper, at col. 2, lines 47-60, states: "[A}pplicant provides an in vivo system for selection of ribozymes targeted to a defined RNA target. The system allows many steps in a selection process for desired ribozymes to be bypassed. In this system, a population of ribozymes having different substrate binding arms (and thus active at different RNA sequences) is introduced into a population of cells including a target RNA molecule. The cells are designed such that only those cells including a useful ribozyme will provide a detectable signal. In this way, a large population of randomly or non-randomly formed ribozyme molecules may be tested in an environment which is close to the true environment in which the ribozyme might be utilized as a therapeutic agent."

Wagner et al. and Draper et al. do not specifically state that their methods do not comprise intervening bacterial cloning steps or that the method does not comprise conformational modeling of mRNA transcribed from the target nucleic acid molecule. However, the prior art discloses methods for assigning function to a transcription product of a target nucleic acid without the need for intervening bacterial cloning steps and conformational modeling.

Gudkov et al. provides methods for designing a retroviral library of nucleic acid fragments to be delivered to eukaryotic cells to test or determine the ability of these nucleic acid fragments to function as genetic suppressor elements (GSE) (see col. 10-12). The methods of Gudkov et al. essentially comprise methods for identifying gene function since the ability of the putative nucleic acid molecules to function, as a GSE is unknown prior to testing. Moreover, the methods of Gudkov et al. do not recite

intervening bacterial cloning steps or conformational modeling as recited in the instant claims.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the teachings of Wagner et al. and Draper et al. with the teachings of Gudkov et al. in the design of the instant invention. One of ordinary skill in the art would have been motivated to make this modification since Wagner et al. and Draper et al. expressly state that their disclosed methods for determining gene function encompass wherein the transfection method comprises the use of retroviral vectors, and the teachings of Gudkov et al. are specifically designed to deliver nucleic acid to cells using retroviral vectors with the express purpose of determining their ability to alter a phenotype of the transfected cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE